ACUTE YELLOW ATROPHY OF THE LIVER AS A SEQUELA TO APPENDECTOMY.[1]

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ACUTE yellow atrophy of the liver is a rare disease; according to Osler about 250 cases are on record. This affection is also called Icterus gravis, Fatal icterus, Pernicious jaundice, Acute diffuse hepatitis, Hepatic insufficiency, etc. Acute yellow atrophy of the liver is characterized by a more or less sudden onset of icterus increasing to the severest form, headaches, insomnia, violent delirium, spasms, and coma. There are often cutaneous and mucous hæmorrhages. The temperature is usually high and irregular. The pulse, first normal, later rapid; urine contains bile pigments, albumen, casts, and products of incomplete metabolism of albumen, leucin, and tyrosin, the presence of which is considered pathognomonic. The affection ends mostly fatally, but there are recoveries on record. The findings of the post-mortem are: liver reduced in size; cut surface mottled yellow, sometimes with red spots (red atrophy), the parenchyma softened and friable; microscopically the liver shows biliary infiltration, cells in all stages of degeneration. Further, we find parenchymatous nephritis, large spleen, degeneration of muscles, hæmorrhages in mucous and serous membranes.

The etiology of this affection is not quite clear. We find the same changes in phosphorus poisoning; many believe it to be of toxic origin, but others consider it to be of an infectious nature; and we have even findings of specific germs (Klebs, Tomkins), of streptococci (Nepveu), staphylococci (Bourdillier), and also the Bacillus coli is found (Mintz) in the affected organs. The disease seems to occur always secondary to some other ailment, and is observed mostly during pregnancy (about one-third of all cases, hence the predominance in women), after

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typhoid fever, recurring typhoid, sepsis, syphilis, gonorrhœa (Aufrecht), sclerema neonatorum, and severe nervous shock (Albu); further on in phosphorus, antimony, and arsenic poisoning. As a sequel to operation, I have found only nine cases of acute yellow atrophy of the liver on record, therefore I consider the following case worthy of relating:

Mr. G. D., twenty years old, brass-worker, from healthy family.

Previous History.—Several times during the last two years, that is, since D. is working as brass polisher, slight lead colics. During the last year twice typical attack of appendicitis. No alcoholism. No venereal diseases.

Present sickness began on December 8, 1901, as another well characterized attack of appendicitis. I saw the young man first, in consultation with Dr. J. G. McAlpine, on December 9, 1901, at 3 P.M., thirty-six hours after onset of the appendicitis. I found temperature 101° F.; pulse, 98. Tongue very dry and coated. Respiration quiet. Face expression good. Abdomen flat. Muscular tension in right side. Ileocæcal region very painful. No dulness on percussion. Patient was somewhat restless and felt chilly. Operation recommended, but delayed, on account of absence of father, until 11.30 P.M. same day, at Detroit Sanitarium. Intramuscular incision. Appendix adherent to side of abdomen. Adhesions broken. Serosa of appendix covered with fibropurulent exudation. Meso-appendix thickened, also cæcum. Ligature of appendix. Stump touched with carbolic acid. Inversion and overstitching impossible, as thread cuts through infiltrated tissue. But as all tissue seemed to be able to recover, the abdominal cavity was closed tight by suture in layers. Operation lasted twenty-five minutes. Chloroform narcosis was tolerated well. Only a small amount of chloroform was used. Pulse after operation, 96.

December 10, 1901. 9 A.M. Temperature, 98.6° F.; pulse, 100. Night: Restless and nauseated. Urine by catheter, eighteen ounces; later, spontaneous. Bowels moved after glycerin injection. Feels generally well. 6 P.M. Temperature, 98.4° F.; pulse, 94.

December 11, 1901. 8 A.M. Temperature, 98.4° F.; pulse, 82. Night: Fairly well. Slight jaundice of skin and conjunc-

tivæ. Several times slight vomiting. Somewhat restless in the afternoon. 8 P.M. Temperature, 97.6° F. (axilla); pulse, 88.

December 12, 1901. 7 A.M. Temperature, 98.8° F.; pulse, 88. Jaundice increased. Hunyádi water vomited. Evening restless and slightly delirious. Vomiting of greenish fluid at 5 P.M. 6 P.M. Temperature, 98° F.; pulse, 84.

December 13, 1901. 8 A.M. Temperature, 98° F.; pulse, 86. All night delirious and very noisy, slept only for short intervals, like in deep coma. Threw about his arms and legs violently. Jaundice increased. Afternoon vomited three times small quantities of black fluid. 5 P.M. Stomach washed out. He was so violent that he had to be held by three men while the stomach was washed. A small amount of brown fluid was found in the stomach, which contained disintegrated red blood-corpuscles. After washing, two ounces saturated solution of Epsom salts were left in the stomach. Stupor continued all day, changing to wild delirium. Bowels moved copiously at night. Bandage changed. Skin suture removed. Wound does not show any reaction, only a little bile-colored serum discharged from same. 7 P.M. Temperature, 100° F.; pulse, 116.

December 14, 1901. Temperature, 100.4° F.; pulse, 108. Delirium and coma seem to increase. Stool and urine involuntarily. No response to loud calling, pinching, pricking, etc. Yelled loudly and threw about his arms and legs. Stool contained bile like in severe chorea. In order to keep him in bed, two men had to hold his limbs all the time, and, as this caused too much strain, legs and arms had to be tied to the bed. Jaundice increased to a deep brown color. Patient swallows food after it is introduced forcibly between the teeth. There was no more vomiting since lavage of stomach. Bromide and codeine given in enema. 8 P.M. Venesection of right median vein, 300 cubic centimetres of blood removed. Intravenous saline infusion of 500 cubic centimetres. 8 P.M. Temperature, 102° F.; pulse, 124.

December 15. 7 A.M. Temperature, 102° F.; pulse, 138. Rested some after venesection. Perspired freely, so that all the bed-clothing was yellow with bile-stained perspiration. Also diuresis seemed to have been freer but involuntarily. Coma and delirium continue. Swallows food like yesterday. Urinated involuntarily. Examination of some urine gained by catheter shows albumen, casts, bile, and crystals of leucin and tyrosin.

Bromides, digitalin, bovinin, and saline solution are given in enema. 8 P.M. Temperature, 98.8° F.; pulse, 106.

December 16. 9 A.M. Temperature, 99.6° F.; pulse, 120. Rested more quietly during the night. Begins to respond a little, but is still mostly in a stupor. Icterus a little lighter. Liver-dulness small, one and one-half inches above rib-bow. Abdomen otherwise flat. Some punctiform hæmorrhages on arms and legs. Wound without any inflammatory symptoms.

From now on all the symptoms decreased in intensity, pulse went down, temperature remained about normal, icterus disappeared gradually, and consciousness returned slowly. Patient got up on the 5th of January, and left the hospital on February 11. At that time there was still some jaundice and small liver-dulness.

Reviewing this record, we have the case of a young brass-worker operated upon for an acute appendicitis. The appendix, cæcum, and omentum were quite inflamed and swollen. The first three days after the operation everything looked favorable except a slight icterus. Then in the fourth night serious delirium developed, very violent spasms set in, only to be interrupted by a deep comatose condition. At the same time deep icterus existed, hæmorrhagic masses were vomited, bile, albumen, casts, leucin, and tyrosin appeared in the urine, the liver-dulness was much diminished. This serious condition lasted five days, to yield finally to a slow improvement.

There can be no doubt but that we had to deal with a case of acute yellow atrophy of the liver after an appendectomy under chloroform. We saw all the typical symptoms: icterus, delirium, spasms, coma, fever, leucin, and tyrosin in the urine. Even the small liver-dulness could be percussed. I think that every one would agree with my diagnosis if I could add to the record of the case an autopsy report! Indeed, recoveries after acute yellow atrophy of the liver are so exceptional, that, for instance, Sajous, *Annual Cyclopædia* (1899, Vol. v, page 395), says, "The disease is so fatal that recovery almost implies a mistake in diagnosis." But, as I mentioned before, there certainly are some recoveries of undoubted cases of this sickness

reported. Weising could gather sixteen cases of favorable termination. I was able to find some more recoveries recorded (Albu, Dobie, Laigne-Lavastine). Senator believes in possibility of recovery, so does Bouchard and others. Nevertheless, the mortality seems to be about 95 per cent.

As already mentioned, very few similar cases after operation are on record. I could find only nine, none of them in this country. The following table will give particulars of these ten cases.

All these ten cases have in common that one or two days after an operation a slight icterus developed, followed by vomiting of sometimes bloody character, serious delirium, coma, and in nine out of ten cases death. Four of the patients were male, three female—in three the sex is not mentioned. Their age varied between twenty and forty-two years. In seven cases chloroform was used as an anæsthetic, once Billroth's chloroform mixture; in two cases the anæsthetic is not named. As predisposing causes alcoholism is given in three cases (Cases 1, 7, and 9); indigestion twice (6 and 8); once with slight catarrhal icterus (6); lead once (10). In one case the affection followed herniotomy with resection of adherent omentum (4); in three cases uterine or adnexa operations; one of them removal of an ovarian cyst with torsion and necrosis of the pedicle (5); one a hysterectomy with morcellement of uterine fibroids (6), and one removal of the adnexa for chronic salpingitis; twice an appendectomy (6 and 10), both cases with inflammation and suppuration, and one time the only operation not abdominal, a very difficult teeth extraction from suppurating jaws (8). The clinical history of Bastianelli's cases was not obtainable; I could not get a copy of his essay and had to content myself with a short excerpt. Autopsies were made in all nine fatal cases and showed every time the serious degenerative condition of the liver, besides nephritis and degeneration of the heart muscle. Multiple punctiform hæmorrhages of mucous membranes were found three times. Mintz found in his case the bacterium coli in the liver parenchyma.

After this analogous experience of six different authors in

TABLE OF CASES OF POSTOPERATIVE ACUTE YELLOW ATROPHY OF THE LIVER.

No.	Author.	Age.	Sex.	Predisposition.	Anæsthetic used.	Operation performed.	Onset of Icterus.	Symptoms.	Result.	Autopsy.
1	Bastianelli.	?	?	?	Chloroform.	?	?	Icterus, vomiting, delirium.	+ between second and tenth day.	Fatty degeneration of heart. Slight nephritis. Punctiform hæmorrhages.
2		?	?	?		?	?			
3		?	?	?		?	?			
4	Bandler.	42	Male.	Alcohol.	Eighty grammes of chloroform.	Herniotomy, with resection of adherent omentum.	One to two days.	Icterus, delirium, coma; temperature, 40° C.	+ on fourth day.	Acute yellow atrophy of liver. Icterus universalis. Multiple hæmorrhages. Nephritis.
5	Stocker.	?	Female.	?	?	Ovarian cyst, with torsion and necrosis of pedicle.	?	?	+	Acute yellow atrophy of liver.
6	Erlach, reported by Bandler.	?	Female.	Catarrh, icterus.	Billroth mixture.	Extirpation of uterus, with morcellement of fibroma.	?	Icterus, delirium.	+	"Atrophia hepatis acuta rubra et flava."
7	Mintz.	40	Male.	Alcohol.	?	Appendicitis, with abscess.	One day.	Icterus, hæmatemesis, convulsions, fever.	+ on sixth day.	Fatty degeneration of heart. Parenchyma. Nephritis. Acute yellow atrophy of liver. Bacterium coli in liver. Erosions in duodenum and stomach.
8	Marten.	34	Female.	Insanity, indigestion.	Seventy c.c. of chloroform in 40 minutes.	Extraction of fourteen teeth from suppurating and necrotic jaw.	One day.	Icterus, vomiting, albumen, casts in urine, delirium, yelling, coma.	+ on fourth day.	Fatty degeneration of heart, kidneys. Acute fatty degeneration of liver.
9	Cohn, of Sonnenburg's Clinic.	21	Female.	Alcohol.	Chloroform.	Salpingo-ovarectomy for pustubes.	Two days.	Icterus, fits of yelling, delirium, albuminuria.	+ on fifth day.	Cloudy swelling of heart, liver, kidneys. Icteric nutmeg liver.
10	Ballin. (Author's case.)	20	Male.	Lead.	Chloroform.	Appendicitis in inflammatory stage; adhesions.	Two days.	Icterus, delirium, coma, fever, bloody vomiting, albumen casts, tyrosinecein in urine.	Recovery.	

ten cases, it is evident that acute yellow atrophy of the liver may occur as one of the rarer complications after operations. Our text-books, some of them with otherwise very exhausting chapters on the complications of the post-operative period, and many special essays on the same topic, do not mention this rare complication at all, at least as far as I have been able to look this up.

As to the etiology of this serious degenerative process in the liver after operations, the few observers disagree in the same line of thought as the authors on the etiology of acute yellow atrophy in general. Some believe it to be of toxic origin; others, of infectious nature. Bandler, Bastianelli, Marten, and Cohn consider the chloroform used in narcosis to be the cause. Mintz found bacterium coli in the affected liver and thrombotic processes in the duodenal arteries, and believes, therefore, in infectious origin. The advocates of the theory that chloroform causes the degenerative process in the liver bring forward many arguments in favor of their opinion. First, a mild icterus after narcosis with chloroform is observed quite often, as first pointed out by Nothnagel in 1866. By experiments on animals, Nothnagel, Toth, Unger and Junker, Stromel, Strassmann, and Ostertag showed beyond doubt that chloroform causes degenerative changes of the liver cells analogous to changes in kidneys and heart muscle. Bandler repeated the same experiments, and compared them with findings after ether inhalations. Chloroform always gave said degenerative changes, ether never.

In men Nothnagel studied first the action of chloroform on the liver, as already mentioned, further on Thiem, Fischer, Fraenkel, and others could always find in cases of chloroform death, degeneration of the liver concurring with destructive changes in kidneys, heart, and muscles. Luther showed on a series of cases that bile in the urine and icterus after chloroform comes and goes with albuminuria. Hence, we have first the clinical observation that chloroform causes sometimes icterus, then we have the proof of autopsies in cases of chloroform death that this anæsthetic can produce degeneration of liver

cells, and finally we have the proof by experiments on animals. Therefore, the conclusion that the acute yellow atrophy in the cases under consideration is simply caused by the chloroform seems to be justified. The experience of our ten tabulated cases shows that chloroform was used seven times; in three cases no mention is made of the anæsthetic used; there is, anyway, as far as I could find out, no such case on record after an ether anæsthesia. But looking over the history of the seven cases,—excepting the three cases of Bastianelli, without an exact clinical history,—we find that in every case an inflammatory condition existed at the time of operation (abscess, appendicitis, torsion of pedicle, etc.). There is no record of any case after an operation in healthy tissue. Six of the operations were laparotomies; only one was outside the abdomen,—the tooth extraction with necrosis of the jaw. This leads to the supposition that infection, furthermore, the handling of inflamed intestines and omentum, is also an important factor. We saw this destructive liver process happen after the same kind of operations after which we meet with thrombosis of the femoral vein, lung infarcts, and other complications of thrombotic and infectious origin. Finally, we must not overlook the fact that some disposition lessening the resistance of the liver cells, as alcoholism, lead or catarrhal jaundice, was recorded in nearly every one of our cases. Considering this, it seems probable that acute yellow atrophy of the liver, after operation, is caused by infectious processes with the help of the toxic influence of chloroform upon the liver. A predisposition by alcohol, etc., as mentioned, seems to be essential as causative factor; however, more observations are needed to clear this etiology. For instance, if some one could report a similar case after ether inhalation, we would have to abandon the idea of chloroform being a causative factor.

In nearly every one of the cases considered we find hæmorrhagic vomiting as a symptom with the malign jaundice. There seems to be some relation between the degenerative process of the liver as described and hæmorrhagic vomiting after operation, as Billroth, von Eiselsberg, Landow, and others

have reported. All the later cases happened after serious laparotomies with omental resections, etc., and their autopsies showed multiple fresh ulcerations of stomach and duodenum, which were also found in Mintz's case of acute yellow atrophy of the liver. Eiselsberg believes the ulceration to be caused by septic thrombotic processes, while Landow considers the chloroform to be their cause. Hæmorrhagic vomiting is observed as a symptom in most cases of acute yellow atrophy of the liver; Landow, on the other hand, observed in one of his cases of hæmatemesis after appendectomy, simultaneously severe icterus, although without delirium. This is the reason that I suspect some relation between the two rare complications of the postoperative period, viz., between the hæmatemesis and the malign jaundice. Maybe both are caused by the same factor, chloroform or infection; maybe the primary changes in both cases are located in the red blood-corpuscles which are essential in carrying the chloroform through the body (Pohl), and also in thrombotic infections. Further observations and experiments will throw light on these questions.

As to the treatment of postoperative yellow atrophy of the liver, our cases give us first a lesson in prophylaxis. The long use of chloroform should be avoided where alcoholism or some other chronic ailment has caused a catarrh of the liver ducts, especially when we have to deal with inflammatory conditions of the viscera. The narcosis, if deemed advisable, can be started with chloroform, but after a short time ether should be substituted; we have to consider that this serious liver affection is at least partially a consequence of chloroform. In a recent publication on "The Accidents of Anæsthesia," Eisendrath supports the same idea by saying, "Chloroform should never be given when it is necessary to administer it for more than an hour, on account of its degenerative effect upon the heart muscle and parenchyma of the liver and kidneys."

If we have to deal with a case of malignant jaundice, the odds are surely against us. Recovery will be the exception. The success in my case I attributed mostly to the venesection and the following intravenous saline infusion. The malign jaundice is the consequence of a destructive liver disease, just

the same as uræmia is a sequela to degenerative processes in the kidneys. The French term for the affection "hepatic insufficiency" characterizes this condition. Considering some good results had with venesection and saline infusion in the treatment of eclampsia, I decided to try the same treatment in my case, which seemed then almost beyond hope. The result was a free diuresis and abundant bile-stained perspiration, just as I had noticed the beneficial influence of the same treatment in uræmia. Bouchard mentioned that all the cases of acute yellow atrophy of the liver which recovered showed this "polyuric crisis," that is, a sudden, large diuresis. Besides the venous infusion after venesection, cathartics, diuretics, and rectal enemata will contribute to the same end, to a speedy and thorough elimination of the toxin produced by the insufficiency of the liver.

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